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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,716	02/16/2006	Masato Kato	18655	8342

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SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
01/28/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,716	KATO ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/5/11*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-13,15,19 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13, 15, 19, and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 1/5/11 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/5/11 has been entered.

Claims 11-13, 15, and 23 have been amended.

Claims 24-27 have been added.

Claims 11-13, 15, 19, and 23-27 are pending and are under examination.

2. Claim 26 is objected to for the following informalities: the claim recites that the graft is "an allograft bone marrow stem cells". Correction is required.

3. In view of Applicant's amendment to the claims, the previous grounds of rejection are withdrawn.

4. The following are new grounds of rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 11-13, 15, 19, and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of down-regulating the immune-activity of an immune competent bone marrow graft and a method of treating a condition characterized by the aberrant,

unwanted, or otherwise inappropriate immuno-activity of an immuno-competent bone marrow graft in a subject comprising administering to said subject or contacting said graft with a monoclonal antibody against CD83, wherein the antibody is not conjugated to a toxic component, and wherein the antibody induces cell lysis
does not reasonably provide enablement for:

A method of down-regulating the immune-activity of an immune competent bone marrow graft and a method of treating a condition characterized by the aberrant, unwanted, or otherwise inappropriate immuno-activity of an immuno-competent bone marrow graft in a subject comprising administering to said subject or contacting said graft iwith a monoclonal antibody fragment against CD83, wherein the antibody fragment is not conjugated to a toxic component, and wherein the antibody fragment induces cell lysis

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP

further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a method of downregulating the immuno-activity of bone marrow graft comprising administering a CD83 antibody, or fragment thereof, wherein the antibody/fragment is not conjugated to a toxic component. The claims specify that the antibodies induce lysis of dendritic cells and/or T cells as the mechanism by which the immuno-activity of graft is downregulated. The instant specification discloses that CD83 monoclonal antibodies can induce cell lysis by an ADCC mechanism. However, ADCC requires the present of an Fc region on the antibody to mediate cell lysis (see Janeway and Travers, page 8:29). Antibody fragments known in the art such as Fab, Fv, sFv do not comprise an Fc region, and would not be expected to function in vivo to deplete CD83+ cells by ADCC mechanisms. Thus, down-regulating the immuno-activity of a graft with an antibody fragment that is not conjugated to a toxic component, by a mechanism which involves depleting CD83 expressing cells, would be highly unpredictable.
Given the unpredictability of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims.

The instant specification demonstrates that CD83 monoclonal antibodies can deplete dendritic cells by an ADCC dependent mechanism, thus inhibiting T cell responses in a mixed lymphocyte reaction. However, the instant specification also demonstrates that a CD83 Fab fragment des not deplete cells or inhibit T cell responses in a mixed lymphocyte reaction. Thus, based on the teachings of the specification, it is apparent that a CD83 fragment, in the absence of conjugation to a toxic component, would not likely induce cell lysis or function to downregulate the immuno-activity of a bone marrow graft, as claimed. Accordingly, it would require undue experimentation to practice the full scope of the claimed invention.

7. Claims 11-13, 15, 19, and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the

application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A method comprising of treating a condition/downregulating the activity of a graft comprising "bone marrow stem cells".

Applicant indicates that support for the new limitations of the claims can be found at pages 26-27 of the specification.

A review of the specification fails to reveal support for the new limitations.

At pages 26-27, the specification discloses various immuno-competent allografts, including bone marrow cells and stem cells. Thus, the specification discloses treating the aberrant immuno-activity of a bone marrow graft or a stem cell graft. A stem cell graft is different than a "bone marrow stem cell" graft, as now claimed, since the specification defines said stem cells as those that can differentiate into all cells (immune and non-immune). While bone marrow stem cells are present in the bone marrow, bone marrow also comprises a variety of other cells at various stages of differentiation include pre- B cells, B, monocytes, T cells, etc. Thus, the scope of a "bone marrow graft", as disclosed by the specification, appears to differ from a "bone marrow stem cell" graft as now claimed.

8. No claim is allowed. Claims 11-13, 15, 19, and 23-27 are free of the prior art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes
Patent Examiner
Technology Center 1600
/Amy E. Juedes/
Primary Examiner, Art Unit 1644